III. Rejection of Claims Under 35 U.S.C. §§ 101/112

Claims 1-4 stand rejected under 35 U.S.C. § 101, and new claims 5-8 are rejected under 35 U.S.. § 101, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The Final Action disagrees with Applicants' logical assertion, based on the evidence, that the sequences of the present invention encodes a novel human membrane protein similar to CD82. In previous responses, Applicants have provided several pieces of evidence that those of skill in the art would find Applicants' assertion credible. That evidence clearly shows that those of skill in the art, in no way affiliated with Applicants, when faced with the same information, would and did identify the sequences of the present invention as a human membrane protein similar to CD82. Thus those of skill in the art agree with Applicants' assertion and would, therefore, clearly find Applicants' assertion credible. Given the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable, this is clear evidence that those skilled in the art would have recognized the function and activity of the protein encoded by the sequences of the present invention, there can, therefore, be no question that Applicants' asserted utility for the described sequences is "credible." According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

The Final Action argues that Applicants have not disclosed a physiological role for said protein. Applicants assert the polypeptide is a novel human membrane protein and in Section 2 of the specification disclosed that membrane proteins play important roles as, *inter alia*, cell surface markers, receptors, and mediators of cell-cell interaction and signal transduction. It is Applicants' position that patentable utility is distinct from, and does not require a knowledge of, physiological function. In fact, historically patentable utility has not required a knowledge of how the invention functions does not require It is also Applicants' position that unless Applicant is claiming a physiological function, evidence of a physiological function is not required to demonstrate patentable utility. In fact, structural claims such as those of the present application are sufficiently supported by structural disclosure as defined by 35 U.S.C. § 101 and related case law. Furthermore, the Action also seems to be implying that

because Applicants' sequence is novel, it lacks utility. Applicants are unaware of any patent law, patent rule, or ruling from the Supreme Court or the Court of Appeals for the Federal Circuit that supports this position. Applicants assertion of the stated utility is legally sufficient and should control the utility analysis unless the Examiner meets the burden of establishing the lack of utility by making evidence of record that conclusively refutes the Applicants asserted utility.

In addition the Final Action submits that SEQ ID NO:1 and 2 of the present invention are not related to CD82, based on the Examiner's finding that they are identical to sequences of a published PCT application WO/200157213-A2. In this PCT application the sequences were identified as BCL-X like. It should be noted that this PCT application and the related US application, was submitted by the Applicants of the present invention and that Applicants are no longer pursuing this application.

The Action also discounts Applicants' assertion regarding the use of the presently claimed polynucleotides on DNA chips, based on the position that such a use would allegedly be generic. Further, the Action seems to be requiring Applicants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Applicants respectfully point out that knowledge of the exact function ~~or role~~ of the presently claimed sequence is not required to track expression patterns using a DNA chip. As set forth in Applicants First Response, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. The claimed sequence provides a specific marker of the human genome (see evidence below), and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, as well as more recently issued U.S. Patent Nos. 5,837,832, 6,156,501 and 6,261,776. Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful.

Additionally, since only a small percentage of the genome (2-4%) actually encodes exons, which in-turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications, further discounting the Examiner's position that such uses are "generic". Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the utility the present

nucleotide sequence has a specific utility in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions, as described in the specification and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences (see evidence below). In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As still further evidence supporting Applicants assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit C**. This is the result of a blast analysis using SEQ ID NO:1 of the present invention when compared to the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded

by 9 exons spread non-contiguously along a region of human chromosome 12,at approximately 12q21. which are contained within partially overlapping clones, AC135034.1, AC025418.23 and AC135034.1. Thus clearly one would not simply be able to identify the 13 protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were.

Finally, the Examiner has determined that applicants argument of due process presented in previous response is not persuasive. Applicants understanding is that issued United States patents retain a legal presumption of validity which in this case indicates that the inventions claimed in the cited patents are *legally presumed* to be in full compliance with the provisions of 35 U.S.C. sections 101, 102, 103, and 112. Applicants respectfully submit that, absent a change in the law as enacted by Congress and signed by the President, it is improper for the Examiner to hold Applicants' invention to a different legal standard of patentability. Given the rapid pace of development in the biotechnology arts, it is difficult for the Applicants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Applicants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Any argument to the contrary is at best arbitrary and at worst capricious. Absent authority provided by an act of Congress or Executive order, arbitrary or capricious conduct by an administrative office the U.S. government has historically proven to conflict with the provisions of the U.S. Constitution. The Patent Office does not have the authority to rewrite U.S. law. However, the Patent Office does have a Constitutional obligation to administer U.S. law in an unbiased and procedurally consistent manner. That is what the Applicants are respectfully requesting the Examiner to consider in the present matter. As the issued U.S. Patents cited above are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph, Applicants respectfully submit that the presently claimed polynucleotide must also meet the requirements of 35 U.S.C. § 101.

For each of the foregoing reasons, Applicants submit that in light of the above discussion and those presented in previous Applicant responses, the presently claimed invention has been shown to

have a substantial, specific, credible and well-established utility and that the rejection of pending claims 1-5 under 35 U.S.C. § 101 has been avoided, and respectfully request that the rejection be withdrawn.

IV Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-8 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse. Applicants submit that as the claims have been shown to have a specific, substantial, credible and well established utility, as detailed in the section above, Applicants respectfully request that the rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, be withdrawn.

V Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

The rejection of claim 2 made under 35 U.S.C. 112, second paragraph, for reciting "... hybridizes under stringent conditions ...," is maintained for the reasons of record. Applicants respectfully disagree. While Applicants submit that the phrase "highly stringent" is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite the exact hybridization wash conditions described as an example in the specification as originally filed. Applicants submit that revised Claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Based on the foregoing, Applicants submit that Claim 2 is sufficiently definite, and respectfully request withdrawal of this rejection.

VI. New Rejection of Claims Under 35 U.S.C. §§ 101

Claims 6 and 8 are rejected under 35 U.S.C. section 101 because the claimed invention is directed to a non-statutory subject matter. This rejection is based on the position that the phrase "a cell" encompasses the cell, as it occurs in nature. For example as a gene therapy patient" (Action at page 7, section 7a). Applicants respectfully traverse. This phrase is contradictory, as a cell as it

occurs in nature in not exemplified by the cells of a gene therapy patient. A gene therapy patient, by definition contains cells that are not as they occur in nature. In fact the role of gene therapy is to alter the activity of the cells of the gene therapy patient.

However, as the action then states that "since Applicants do not intend to claim a naturally occurring products amendment of the claims to show the hand of man would obviate this rejection", Applicants assume that this rejection is based on the position that the phrase "a cell" can encompass the cell, as it occurs in nature. Applicants invite the Examiners attention to the wording of claims 6 and 8.

Claim 6. A cell comprising the expression vector of Claim 5.

Claim 8. A cell comprising the expression vector of Claim 7.

While it is true that the phrase "a cell" can encompass a cell as it occurs in nature, the wording of dependent claims 6 and 8 of the present invention clearly limits the claimed invention to a cell comprising the expression vector of claims 5 and 7. Applicants respectfully submit that cells, as they occur in nature do not normally contain the expression vectors of claims 5 or 7. Therefore, Applicants respectfully request that this rejection be withdrawn.

VII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Hamud have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

This response is timely filed and Applicants believe no fees are due in connection with this response. However, should this be incorrect the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

Respectfully submitted,

April 30, 2003
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